PATENT SPECIFICATION (11) 1285350

1285350

NO DRAWINGS

(21) Application No. 57940/69 (22) Filed 26 Nov. 1969
(61) Patent of Addition to No. 1207371 dated 29 Aug. 1967
(31) Convention Application No. 175375 (32) Filed 26 Nov. 1968 in
(33) France (FR)
(45) Complete Specification published 16 Aug. 1972
(51) International Classification C07C 61/04
(52) Index at acceptance
C2C 3A10A4F 3A10A5E 3A10A5K 3A10E3C1 3A10E5E

(54) CYCLOPROPANE CARBOXYLIC ACID DERIVATIVES

(71) We, ROUSSEL UCLAF, a French Body Corporate, of 35, Boulevard des Invalides, Paris 7e, France, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention is concerned with improvements in or relating to the preparation of cyclopropane-1-carboxylic acids, and is an improvement in, or modification of, the invention described and claimed in our copending Application No. 39542/67 (Serial No. 1,207,371).

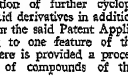
Our copending Patent Application No. 39542/67 (Serial No. 1,207,371) describes and claims certain cyclopropane-1-carboxylic acids and esters thereof, *inter alia* racemic *trans* - 3,3 - dimethyl - 2 - cyclopentylidene-methyl - cyclopropane - 1 - carboxylic acid and its two optically active isomers, racemic *trans* - 3,3 - dimethyl - 2 - (2' - ethyl - 1'-butenyl) - cyclopropane - 1 - carboxylic acid, racemic *trans* - 3,3 - dimethyl - 2 - cyclopropylidene - methyl - cyclopropane - 1-carboxylic acid and racemic *trans* - 3,3 - dimethyl - 2 - cyclobutylidene - methyl - cyclopropane - 1 - carboxylic acid, the esters of these specific compounds having valuable insecticidal properties.

The said Patent Application further described and claims a general process for the preparation of the said cyclopropane-1-carboxylic acids and esters thereof which involves the reaction of an alkyl β,β-dimethyl acrylate with an appropriate phenylsulphone, and, if desired, hydrolysis of the resulting ester to produce the free acid which may, if desired, be subsequently resolved into its component optical isomers. For example, racemic *trans*-3,3 - dimethyl - 2 - cyclopentylidene - methyl-cyclopropane - 1 - carboxylic acid can be resolved in accordance with the method described in the said Application, by formation of the 1-ephedrine salt.

The said Application further describes and claims an additional process which is especially advantageous for the preparation of cyclopropane-1-carboxylic acids substituted in the 2-position by a cyclopropylidene-methyl or cyclobutylidene-methyl radical. This additional process involves the reaction in a basic medium of a cyclopropyl or cyclobutyl triaryl phosphonium halide with racemic *trans*-caronaldehydic acid.

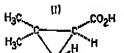
We have now discovered that the last-mentioned process is capable of a wider application than was hitherto appreciated and that it can be advantageously employed for the preparation of further cyclopropane-1-carboxylic acid derivatives in addition to those referred to in the said Patent Application.

According to one feature of the present invention there is provided a process for the preparation of compounds of the general formula

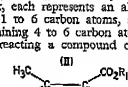


(I)

(in which R' represents the grouping



(wherein R_2 and R_3, which may be the same or different, each represents an alkyl radical containing 1 to 6 carbon atoms, an alkylene chain containing 4 to 6 carbon atoms) which comprises reacting a compound of formula



(II)

(in which R_2 represents a hydrogen atom or an alkyl radical containing 1 to 4 carbon atoms) with a phosphonium salt of partial formula

III

(in which R_2 and R_3 are as hereinbefore defined) in the presence of a strong base, and (when R_1 represents an alkyl radical) hydrolysing the resulting ester to produce a compound of formula I.

The hydrolysis of the resulting ester in the above-described process according to the invention is conveniently effected under basic conditions.

The process according to the present invention is generally applicable to the preparation of compounds of formula I having either the (1R, 2R) or (1S, 2S) configuration, as well as racemic mixtures of such compounds.

The rotatory power of the optionally active acids of formula I is relatively low and these acids have therefore been defined according to the absolute configuration of their asymmetric carbons in the 1- and 2-positions in accordance with the nomenclature of R. S. CAHN, Sir C. Ingold and V. PRELOG [Expérientia 12, 81 (1956) and Angew. Chem. 78, 413 (1966)].

Thus, for example, according to this nomenclature, *d - trans* - 3,3 - dimethyl - 2-cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid (acid A_1), $[\alpha]_D = +2°$ (c= 1%, chloroform) and *l - trans* - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1 - carboxylic acid (acid B_1), $[\alpha]_D = 0°$ (c=1%, chloroform), described in Patent Application No. 39542/67 may be designated respectively *trans* - 3,3 - dimethyl-2 - cyclopentylidene - methyl - cyclopropane-1 - carboxylic acid (1R, 2R) (acid A_1) and *trans* - 3,3 - dimethyl - 2 - cyclopenylidene-methyl - cyclopropane - 1 - carboxylic acid (1S, 2S) (acid B_1).

It will be appreciated that in the presence of the strong base employed in the process according to the invention the above-identified phosphonium salt of formula III will be present in the reaction medium in the form of an ylide of formula:—

IIIa

The process according to the present invention offers in comparison with the process involving sulphones described in the above-mentioned Patent Application, the advantage of obtaining direct access to the compounds of formula I having the (1R, 2R) or (1S, 2S) configuration by using as starting materials of formula II, aldehydes of the (1R, 2R) or (1S, 2S) configuration respectively without having recourse to a resolution of the final product. Moreover, the compounds of formula I of (1R, 2R) or (1S, 2S) configuration so obtained are not contaminated by their optical isomer and are thus obtained in a good state of purity.

Furthermore, it has also been discovered that proceeding by way of the alkyl 1-carboxylates of formula I, enables particularly pure products to be obtained by physical means, such as a redistillation.

The phosphonium salt of formula III (as hereinbefore defined) is advantageously a triaryl phosphonium salt (e.g. a triphenylphosphonium salt), or a tris-(dialkylamino) phosphonium, [(bis - dialkylamino) - aryl] phosphonium or (dialkylamino - diaryl) phosphonium salt, all of these salts being converted to an ylide of formula IIIa, under the action of strong bases. The phosphonium salt is preferably a phosphonium halide, e.g. the iodide or bromide.

The strong base employed in the process according to the invention is advantageously an alkali metal hydride, amide or alcoholate, e.g. sodium methoxide, or an alkyllithium, e.g. butyl-lithium.

The reaction of the aldehyde of formula II is conveniently effected in an organic solvent, e.g. diethyleneglycol monomethyl ether, diethyleneglycol diethyl ether, ethyl ether, dimethylsulphoxide, dimethylformamide, tetrahydrofuran, dimethoxyethane or benzene.

It has been found especially advantageous to employ either an alkali-metal alcoholate in the presence of dimethylsulphoxide or an alkyllithium in the presence of dimethoxyethane or benzene.

The crude reaction product of the process according to the invention may, if desired, be purified by conventional methods. For example, the reaction product can be treated with Girard reagent T in order to remove, by solubilisation in the aqueous phase, the unreacted aldehyde fraction. Alternatively, for example, the reaction product can be purified by trituration or recrystallisation in a suitable solvent.

When the starting aldehyde is an ester, (i.e. when R_1 in formula II represents an alkyl radical) the crude reaction product obtained by the process according to the invention can be purified by subjecting it to redistillation.

The crude acid obtained in the process of the invention can be purified by reaction with an orangic base, and if desired, crystal-

lisation of the resulting salt. The free acid can then be recovered by the addition of a strong acid.

Thus, for example, in order to purify crude (1R, 2R) *trans* - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid, it is advantageous to convert the crude acid into the 1-ephedrine salt thereof, which can subsequently be purified by crystallisation in, for example, ethyl acetate.

The use of the salts of acids of formula I with optically active bases, referred to above, is in this case only a convenient method of eliminating reaction impurities.

The alkyl radical represented by R_1 in formula II is preferably a methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl or *t*-butyl radical.

The racemic, (1R, 2R) and (1S, 2S) *trans*-3,3 - dimethyl - 2 - formyl - cyclopropane-1 - carboxylic acids and their alkyl esters of formula II employed as starting materials in the process according to the invention can be conveniently prepared by the reaction of ozone with the respective racemic, (1R, 2R) or (1S, 2S) chrysanthemic acid or alkyl esters thereof, and subsequent reduction of the resulting compound with dimethyl sulphide, as described in our copending Patent Application No. 35377/69 (Serial No. 1,283,225); the reaction of the ozone and chrysanthemic acid is advantageously effected at —80°C and preferably in a methanol solvent. The preparation of 3,3 - dimethyl - 2 - formyl-cyclopropane - 1 - carboxylic acid (1R, 2R), is described hereinafter by way of example.

Racemic, (1R, 2R) or (1S, 2S) aldehydes of formula II in which R_1 represents a hydrogen atom can, if desired, be obtained by saponification of their corresponding alkyl esters, or by applying the processes described by M. MATSUI *et al* [Agr. Biol. Chem., Vol. 27, No. 8, 554 (1963)] or RYO YAMAMOTO [Scient. Papers Inst. Phys. Chem. Res. 3, 193 (1925)].

For a better understanding of the invention, the following Examples are given by way of illustration only.

Preparation

(1R, 2R) trans - 3,3 - dimethyl - 2 - formyl-cyclopropane - 1 - carboxylic acid

30 g. of (1R, 2R) *d-trans*-chrysanthemic acid were dissolved in 375 c.c. of methanol, the temperature of the mixture brought to —80°C and an ozonised oxygen current bubbled into the reaction medium until a blue colouration appeared; a current of oxygen was bubbled in for fifteen minutes and then a current of nitrogen for forty-five minutes. 15 c.c. of dimethyl sulphide were slowly added to the resulting mixture which was maintained for thirty minutes at about —35°C, then for one hour at 0°C and finally for one hour at ambient temperature. The methanol was removed by distillation under reduced pressure and the residue introduced in a solution of 25.5 g. of trimethylamino acetohydrazide chloride (reagent T) in 250 c.c. of ethanol and 25 c.c. of acetic acid. The reaction mixture was refluxed, being kept under reflux for one hour, then cooled and poured into a dilute solution of caustic soda. The resulting mixture was extracted with ether in order to remove the non-aldehydic fraction, the resulting mixture acidified with a dilute aqueous solution of hydrochloric acid, the acid aqueous phase extracted with ether and the ethereal solutions washed, dried and concentrated to dryness. The residue was triturated with petroleum ether (b.p.=35°—75°C) and 8.7 g. of (1R, 2R) *trans* - 3,3 - dimethyl - 2 - formyl-cyclopropane - 1 - carboxylic acid was obtained.

(1R, 2R) *D-trans* chrysanthemic acid can be obtained starting from *dl-trans-cis* chrysanthemic acid by insolubilisation of its D-(—) - threo - 1 - *p* - nitrophenyl - 2 - dimethylaminopropane - 1,3 - diol salt, according to the process described in our copending Patent Application No. 32550/68 (Serial No. 1,220,160).

In an analogous way starting from (1S, 2S) *l-trans*-chrysanthemic acid, (1S, 2S) *trans*-3,3 - dimethyl - 2 - formyl - cyclopropane-1 - carboxylic acid was obtained.

(1S, 2S) *l-trans* chrysanthemic acid was obtained starting from *dl-trans-cis* chrysanthemic acid by insolubilisation of its L-(+) - threo - 1 - *p* - nitrophenyl - 2 - dimethylaminopropane - 1,3 - diol salt, according to the process described in our copending Patent Application No. 32550/68 (Serial No. 1,220,160).

EXAMPLE 1

(1R, 2R) trans - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid

24.66 g. of triphenylcyclopentyl-phosphonium bromide, then gradually 97 c.c. of a 1.9 N solution of butyllithium in hexane were introduced in 100 c.c. of dimethoxyethane under an atmosphere of nitrogen. The reaction mixture was agitated for two hours at ambient temperature, and, without exceeding 60°C, 5.7 g. of (1R, 2R) *trans* - 3,3 - dimethyl - 2 - formyl - cyclopropane - 1-carboxylic acid in solution in 30 c.c. of dimethoxyethane were introduced therein. After agitation for two hours at 60°C, the reaction mixture was cooled and concentrated to dryness by distillation under reduced pressure. Water was added to the residue, the mixture agitated and the aqueous phase extracted with ether. After removal of the ethereal extracts, the aqueous phase was acidified with dilute hydrochloric acid up to pH=4.7 and the acid aqueous phase extracted with ether. The combined ethereal extracts were washed with

water, dried and concentrated under reduced pressure to yield an oil.

This oil was introduced in a solution of 10 g. of trimethylamino acetohydrazide chloride (reagent T) in 100 c.c. of ethanol and 20 c.c. of acetic acid, the reaction mixture taken to reflux and kept there for one hour. After cooling the resulting mixture was made alkaline with an aqueous solution of caustic soda, the aqueous mother liquors extracted with ether and the combined ethereal extracts dried and the solvent evaporated under reduced pressure to yield 3.85 g. of crude acid.

This crude acid was dissolved in 11 c.c. of ethyl acetate, and 3.2 g. of l-ephedrine dissolved in 11 c.c. of ethyl acetate was added to the solution. After leaving for a while, the precipitate thus formed was isolated by suction-filtering to yield 5.55 g. of the l-ephedrine salt of (1R, 2R) *trans*-3,3-dimethyl-2 - cyclopentylidene - methyl - cyclopropane-1 - carboxylic acid, m.p.=158°C which is then recrystallised from ethyl acetate, m.p.=160°C, $[\alpha]_D$=−6° (c=0.25%, chloroform).

The purified product was acidified with a dilute aqueous solution of hydrochloric acid, the acid aqueous phase extracted with ether and the ethereal extracts washed with water, dried and concentrated to dryness under reduced pressure. After crystallisation by the addition of a small quantity of petroleum ether, there are obtained 2.70 g. of (1R, 2R) *trans* - 3,3 - dimethyl - 2 - cyclopentylidene-methyl - cyclopropane - 1 - carboxylic acid, m.p.=about 35°C, $[\alpha]_D^{26}$=+5° (c=0.35%, chloroform).

N.M.R. Spectrum (deuterochloroform):

The N.M.R. spectrum displays the following characteristics:

—peaks at 71 and 79 hz, corresponding to the methyl hydrogens at the 3-position;

—peaks at 82.5 and 87.5 hz, corresponding to the hydrogen at the 1-position (doublet),

—peaks at 100 and 135 hz, corresponding to the hydrogens of the cyclopentane ring,

—peak at 695 hz, corresponding to the carboxyl hydrogen.

This compound is identical to that described in our copending Patent Application No. 39542/67 (Serial No. 1,207,371) under the name of *d* - *trans* - 3,3 - dimethyl - 2-cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid or A_1 acid.

Triphenylcyclopentylphosphonium bromide can be obtained by the method of F. RAMIREZ and S. LEVY J. Am. Chem. Soc., 79, 67 (1957).

In the same way, starting from (1S, 2S) *trans* - 3,3 - dimethyl - 2 - formyl - cyclopropane - 1 - carboxylic acid, (1S, 2S) trans-3,3 - dimethyl - 2 - cyclopentylidene - methyl-cyclopropane - 1 - carboxylic acid, $[\alpha]_D^{26}$=0° (c=1%, chloroform) was prepared, identical to that described in our copending Patent Application No. 39542/67 (Serial No. 1,207,371) under the name of *l* - *trans* - 3,3-dimethyl - 2 - cyclopentylidene - methyl-cyclopropane - 1 - carboxylic acid or B_1 acid.

EXAMPLE 2

(1R, 2R) trans - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid

86.5 g. of triphenylcyclopentyl - phosphonium bromide, then gradually 340 c.c. of a 1.3 N solution of butyllithium in hexane were introduced into 350 c.c. of dimethoxyethane under an atmosphere of nitrogen. The reaction mixture was agitated for two hours at ambient temperature and without exceeding 60°C, 20 g. of (1R, 2R) *trans* - 3,3-dimethyl - 2 - formyl - cyclopropane - 1-carboxylic acid in solution in 105 c.c. of dimethoxyethane were introduced therein. The mixture was agitated for two hours at 60°C, cooled and concentrated to dryness by distillation under reduced pressure. Water was added to the residue, the mixture agitated and the aqueous phase extracted with ether. The ethereal extracts were removed, the aqueous phase acidified with dilute hydrochloric acid up to pH=4.7, and the acid aqueous phase extracted with ether. The combined ethereal extracts were washed with water, dried and the solvent evaporated under reduced pressure to yield an oil which was then admixed with 80 c.c. of ethyl acetate. The precipitate thus formed was isolated by suction-filtering, washed with ethyl acetate and 21 g. of crude acid obtained.

A solution of 22.5 g. of l-ephedrine in 90 c.c. of ethyl acetate was added to the 21 g. of crude acid.

After leaving to crystallise, the precipitate thus formed was isolated by suction-filtering, washed with ethyl acetate and dried to yield 27 g. of l-ephedrine salt of (1R, 2R) *trans*-3,3 - dimethyl - 2 - cyclopentylidene - methyl-cyclopropane - 1 - carboxylic acid, m.p.=160°C, $[\alpha]_D^{26}$=−5.5° (c=0.35%, chloroform).

After acidification of this l-ephedrine salt, according to the same method as in example 1, (1R, 2R) *trans* - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid was obtained in an almost quantitative yield based on the ephedrine salt.

EXAMPLE 3

(1R, 2R) trans - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid

Stage A:

(1R, 2R) methyl trans - 3,3 - dimethyl - 2-cyclopentylidene - methyl - cyclopropane - 1 - carboxylate

53 g. of triphenylcyclopentyl - phos-

phonium bromide [(the compound obtained according to FAUSTO RAMIREZ and STEPHEN LEVY J. Am. Chem. Soc. 79, 67 (1957)] and 11.6 g. of sodium methoxide were introduced into 160 c.c. of dimethylsulphoxide under an inert atmosphere. The mixture was agitated for 1 hour at ambient temperature and 13.4 g. of methyl (1R, 2R) *trans* - 3,3 - dimethyl - 2 - formyl - cyclopropane - 1 - carboxylate (the compound obtained according to our copending Patent Application No. 35377/69 (Serial No. 1,283,225) introduced therein in the course of 30 minutes. The reaction mixture was agitated for 21 hours at ambient temperature and poured into a mixture of ice and an aqueous solution of hydrochloric acid. After addition of cyclohexane, the mixture was agitated, insoluble matter (triphenylphosphine oxide) eliminated by filtering, the organic phase separated by decanting and the aqueous phase extracted with cyclohexane. The combined organic phases were washed successively with water, an aqueous solution of sodium bicarbonate and then again water and the resulting organic solution dried and concentrated to dryness by distillation under reduced pressure. The residue was redistilled to yield 17.29 g. of methyl (1R, 2R) *trans* - 3,3 - dimethyl - 2 - cyclopentylidene-methyl - cyclopropane - 1 - carboxylate, b.p.: 0.5 mm/Hg=82°C, $[\alpha]_D = +5°$ (c=1%, chloroform).

The saponification value of this compound is 271 mg. of caustic potash per gram (theory 269).

N.M.R. Spectrum (deuterochloroform)

The N.M.R. spectrum displays the following characteristics:

—peaks at 43—44 hz corresponding to hydrogen at the 1-position;

—peaks at 70—77 hz corresponding to the methyl hydrogens at the 3-position;

—peaks at 95—105 and 130—140 hz corresponding to the hydrogens of the cyclopentane ring.

—peaks at 227 hz corresponding to methyl hydrogen of the methoxycarbonyl radical,

—peaks at 295.5—305.5 hz corresponding to the methyl hydrogen of the cyclopentylidene methyl radical.

State B:

(1R, 2R) trans - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid

10 g. of methyl (1R, 2R) *trans* - 3,3 - dimethyl - 2 - cyclopentylidene - methyl-cyclopropane - 1 - carboxylate, then 5 c.c. of an aqueous solution of 10 N caustic potash were introduced into a mixture of 10 c.c. of methanol and 10 c.c. of water under an inert atmosphere. The resultant reaction mixture was taken to reflux, kept there from 1 hour and 30 minutes and the methanol removed by distillation under normal pressure. After addition of water and isopropyl ether, the reaction mixture was acidified by the addition of an aqueous solution of hydrochloric acid, the organic phase separated by decanting, the aqueous phase extracted with isopropyl ether and the combined organic phases washed with water and concentrated to dryness under reduced pressure to yield 9.25 g. of (1R, 2R) *trans* - 3,3 - dimethyl - 2 - cyclopentylidene - methyl - cyclopropane - 1-carboxylic acid $[\alpha]_D = +5°$ (c=0.35%, chloroform).

N.M.R. Spectrum (deuterochloroform)

The N.M.R. spectrum displays the following characteristics:

—peaks at 71 and 79 hz corresponding to the methyl hydrogens at the 3-position;

—peaks at 82.5 and 87.5 hz corresponding to the hydrogen in the 1-position (doublet);

—peaks at 100 and 135 hz, corresponding to the hydrogens of the cyclopentane ring;

—peak at 695 hz corresponding to the carboxyl hydrogen.

In an analogous way, starting from the methyl esters of (1S, 2S) or racemic *trans*-3,3 - dimethyl - 2 - formyl - cyclopropane-1 - carboxylic acids, (1S, 2S) or racemic *trans* - 3,3 - dimethyl - 2 - cyclopentylidene-methyl - cyclopropane - 1 - carboxylic acids were obtained.

EXAMPLE 4

(1R, 2R) trans - 3,3 - dimethyl - 2 - (2'-ethyl - 1' - butenyl) - cyclopropane - 1-carboxylic acid

Stage A:

Methyl ester of (1R, 2R trans - 3,3 - dimethyl - 2 - (2' - ethyl - 1' - butenyl)-cyclopropane - 1 - carboxylic acid

23 g. of triphenyl - 3 - pentyl - phosphonium iodide were introduced into 200 c.c. of benzene under an inert atmosphere, 29.8 c.c. of 1.68 N hexane solution of butyllithium added thereto and the mixture agitated for 2 hours at ambient temperature. A solution of 9.15 g. of methyl ester of (1R, 2R) *trans* - 3,3 - dimethyl - 2 - formyl-cyclopropane - 1 - carboxylic acid in 20 c.c. of benzene was slowly introduced and the mixture agitated for 2 hours at ambient temperature. After the addition of water, the mixture was filtered to eliminate insoluble matter, the organic phase separated by decanting and the aqueous phase extracted with ether. The combined organic phases were dried, concentrated to dryness by distillation under reduced pressure and petroleum ether (b.p. 65—75°C) added to the residue. After removal of the insoluble matter thus formed (triphenyl phosphine oxide) by filtering, the residue was concentrated to dryness by distillation under reduced pressure to yield 9.67

g. of methyl ester of (1R, 2R) *trans* - 3,3-dimethyl - 2 - (2' - ethyl - 1' - butenyl)-cyclopropane - 1 - carboxylic acid.

Stage B:

(1R, 2R) trans - 3,3 - dimethyl - 2 - (2'-ethyl - 1' - butenyl) - cyclopropane - 1-carboxylic acid

9.67 g. of methyl ester of (1R, 2R) *trans*-3,3 - dimethyl - 2 - (2' - ethyl - 1' - butenyl)-cyclopropane - 1 - carboxylic acid were introduced into a mixture of 70 c.c. of methanol and 35 c.c. of 2 N aqueous solution of caustic soda under an inert atmosphere and the reaction mixture taken to reflux, kept there for 2 hours and the methanol removed by distillation. After the addition of water, the aqueous phase was extracted with ether, the ethereal washings removed, the aqueous phase acidified with an aqueous solution of hydrochloric acid and the acid aqueous phase extracted with ether. The combined ethereal phases were dried, concentrated to dryness by distillation and the residue redistilled under reduced pressure. The middle fraction of the distillation (weight: 5.87 g., b.p.=96°C under 0.15 mm/Hg) was dissolved in a mixture of 50 c.c. of ethanol and 5 c.c. of acetic acid, 5 g. of reagent T (trimethylaminoacetohydrazide chloride) added thereto and the reaction mixture taken to reflux and kept there for 1 hour and 30 minutes. After cooling, the reaction mixture was poured into a dilute aqueous solution of caustic soda, the aqueous phase extracted with ether and the combined ethereal phases dried and concentrated to dryness by distillation to yield 5.05 g. of (1R, 2R) *trans* - 3,3 - dimethyl - 2 - (2'-ethyl - 1' - butenyl) - cyclopropane - 1-carboxylic acid, $[\alpha]_D = +28.5°$ ($c = 1.4\%$, ethanol).

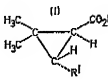
U.V. Spectrum (ethanol)
max. at 200—201 nm ($E_{1\,cm}^{1\%}$: 611)

N.M.R. Spectrum (deuterochloroform)
The N.M.R. spectrum displays the following characteristics:

—peaks at 51.5—59—66 hz corresponding to the methyl hydrogens of the 2'-ethyl butenyl radical;
—peaks at 69.0—78.5 hz corresponding to the methyl hydrogens at the 3-position;
—peaks at 81—86 hz corresponding to the hydrogen at the 1-position;
—peaks at 124 hz corresponding to the CH_2 of the 2'-ethyl butenyl radical;
—peaks at 287—295 hz corresponding to the ethylene hydrogen of the butenyl radical;
—peaks at 676 hz corresponding to the carboxyl hydrogen.

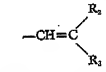
WHAT WE CLAIM IS:—

1. A process for the preparation of compounds of the general formula

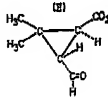


(I)

in which R' represents the grouping



(wherein R_4 and R_5, which may be the same or different, each represents an alkyl radical containing 1 to 6 carbon atoms or R_4 and R_5 together represent an alkylene chain containing 4 to 6 carbon atoms) which comprises reacting a compound of formula



(II)

(in which R_1 represents a hydrogen atom or an alkyl radical containing 1 to 4 carbon atoms) with a phosphonium salt of partial formula

III

(in which R_2 and R_3 are as hereinbefore defined) in the presence of a strong base, and (when R_1 represents an alkyl radical) hydrolysing the resulting ester to produce a compound of formula I.

2. A process as claimed in Claim 1 in which the hydrolysis of the said resulting ester is effected under basic conditions.

3. A process as claimed in Claim 1 or Claim 2 in which the phosphonium salt of partial formula III is a triaryl-phosphonium salt.

4. A process as claimed in claim 3 in which the triaryl-phosphonium salt is a triphenylphosphonium salt.

5. A process as claimed in Claim 1 or Claim 2 in which the phosphonium salt of partial formula III is a tris-(dialkylamino) phosphonium salt.

6. A process as claimed in Claim 1 or

Claim 2 in which the phosphonium salt of partial formula III is a [(bis-dialkylamino)-aryl] phosphonium salt.

7. A process as claimed in Claim 1 or Claim 2 in which the phosphonium salt of partial formula III is a (dialkylamino-diaryl) phosphonium salt.

8. A process as claimed in any of the preceding claims in which the phosphonium salt of partial formula III is a phosphonium halide.

9. A process as claimed in Claim 8 in which the phosphonium halide is a phosphonium iodide or bromide.

10. A process as claimed in any of the preceding claims in which the strong base is an alkali metal hydride, amide or alcoholate or an alkyl-lithium.

11. A process as claimed in Claim 10 in which the strong base is sodium methoxide or butyl-lithium.

12. A process as claimed in any of the preceding claims in which the reaction is effected in an organic solvent.

13. A process as claimed in Claim 12 in which the organic solvent comprises diethyleneglycol monomethyl ether, diethyleneglycol diethyl ether, ethyl ether, dimethylsulphoxide, dimethylformamide, tetrahydrofuran, dimethoxyethane or benzene.

14. A process as claimed in any of the preceding claims for the preparation of a compound of formula I having the (1R, 2R) or (1S, 2S) configuration wherein the compounds of formula II has the (1R, 2R) or (1S, 2S) configuration respectively.

15. A process as claimed in Claim 1 substantially as herein described.

16. A process for the preparation of *trans*-3,3 - dimethyl - cyclopropane - 1 - carboxylic acid derivatives substantially as herein described in any of the Examples.

17. Compounds of general formula I (as defined in Claim 1) whenever prepared by a process as claimed in any of the preceding claims.

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Printed for Her Majesty's Stationery Office, by the Courier Press, Leamington Spa, 1972.
Published by The Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.